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NEWS	15	MAR 31	CAS REGISTRY enhanced with additional experimental spectra
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L1 173 (RNA POLYMERASE II) (4A) PHOSPHATASE

=> s (human or sapien) (4A) phosphatase
L2 19583 (HUMAN OR SAPIEN) (4A) PHOSPHATASE

=> s l1 and l2
L3 23 L1 AND L2

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L4 20 DUPLICATE REMOVE L3 (3 DUPLICATES REMOVED)

=> d l4 bib ab

L4 ANSWER 1 OF 20 MEDLINE on STN DUPLICATE 1
AN 2007466356 MEDLINE
DN PubMed ID: 17487459
TI Expression and characterization of HSPC129, a RNA
polymerase II C-terminal domain phosphatase.
AU Qian Hui; Ji Chaoneng; Zhao Shuo; Chen Jinzhong; Jiang Mei; Zhang Yong;
Yan Mi; Zheng Dan; Sun Yaqiong; Xie Yi; Mao Yumin
CS State Key Laboratory of Genetic Engineering, Institute of Genetics, School
of Life Sciences, Fudan University, Room 602, Science Building, Shanghai,
PR China.
SO Molecular and cellular biochemistry, (2007 Sep) Vol. 303, No. 1-2, pp.
183-8. Electronic Publication: 2007-05-09.
Journal code: 0364456. ISSN: 0300-8177.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200710
ED Entered STN: 10 Aug 2007
Last Updated on STN: 19 Oct 2007
Entered Medline: 18 Oct 2007

AB Phosphorylation status of RNA polymerase (RNAP) II's largest subunit C-terminal domain (CTD) plays an important role during transcription cycles. The reversible phosphorylation mainly occurs at serine 2 and serine 5 of CTD heptapeptide repeats and regulates RNAP II's activity during transcription initiation, elongation and RNA processing. Here we expressed and characterized HSPC129, a putative human protein bearing a CTD phosphatase domain (CPD). PCR analysis showed that it was ubiquitously expressed. HSPC129DeltaTM, the truncate HSPC129 with first 156 N terminal amino acids deleted, exhibited Mg(2+) dependent phosphatase activity at pH 5.0. Its specific CTD phosphatase activity was verified in vitro. Our research suggests that HSPC129 may regulate the dynamic phosphorylation of RNAP II CTD.

=> d 14 1-20 bib ab

L4 ANSWER 1 OF 20 MEDLINE on STN DUPLICATE 1
AN 2007466356 MEDLINE
DN PubMed ID: 17487459
TI Expression and characterization of HSPC129, a RNA polymerase II C-terminal domain phosphatase.
AU Qian Hui; Ji Chaoneng; Zhao Shuo; Chen Jinzhong; Jiang Mei; Zhang Yong; Yan Mi; Zheng Dan; Sun Yaqiong; Xie Yi; Mao Yumin
CS State Key Laboratory of Genetic Engineering, Institute of Genetics, School of Life Sciences, Fudan University, Room 602, Science Building, Shanghai, PR China.
SO Molecular and cellular biochemistry, (2007 Sep) Vol. 303, No. 1-2, pp. 183-8. Electronic Publication: 2007-05-09.
Journal code: 0364456. ISSN: 0300-8177.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200710
ED Entered STN: 10 Aug 2007
Last Updated on STN: 19 Oct 2007
Entered Medline: 18 Oct 2007
AB Phosphorylation status of RNA polymerase (RNAP) II's largest subunit C-terminal domain (CTD) plays an important role during transcription cycles. The reversible phosphorylation mainly occurs at serine 2 and serine 5 of CTD heptapeptide repeats and regulates RNAP II's activity during transcription initiation, elongation and RNA processing. Here we expressed and characterized HSPC129, a putative human protein bearing a CTD phosphatase domain (CPD). PCR analysis showed that it was ubiquitously expressed. HSPC129DeltaTM, the truncate HSPC129 with first 156 N terminal amino acids deleted, exhibited Mg(2+) dependent phosphatase activity at pH 5.0. Its specific CTD phosphatase activity was verified in vitro. Our research suggests that HSPC129 may regulate the dynamic phosphorylation of RNAP II CTD.

L4 ANSWER 2 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:1356154 CAPLUS
DN 146:94691
TI Gene map of human genes, single nucleotide polymorphisms, and haplotypes associated with longevity
IN Belouchi, Abdelmajid; Raelson, John Verner; Bradley, Walter Edward; Paquin, Bruno; Nguyen-Huu, Quynh; Croteau, Pascal; Allard, Rene; Cousineau, Johanne; Paquin, Nouzha; Van Eerdewegh, Paul; Little, Randall David; Keith, Tim; Segal, Jonathan
PA Genizon Biosciences, Inc., Can.

SO PCT Int. Appl., 219pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006138696	A2	20061228	WO 2006-US23724	20060619
	WO 2006138696	A3	20070607		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
	CA 2612389	A1	20061228	CA 2006-2612389	20060619
PRAI	US 2005-691309P	P	20050617		
	WO 2006-US23724	W	20060619		

AB The present invention relates to the selection of a set of single nucleotide polymorphism (SNP) markers for use in genome-wide association studies based on linkage disequil. mapping. of a Quebec founder population. Genotyping was performed using the Perlegen Life Sciences ultra-high-throughput platform and allele discrimination through allele-specific hybridization. In total, 248,535 SNPs, spread over 3 microarrays, were genotyped. The raw data generated by the genome-wide association was analyzed by various means to identify candidate regions associated with longevity. A series of gene characterization steps was performed for each candidate region; any gene or EST mapping to the interval based on public map data or proprietary map data was considered as a candidate longevity gene. Candidate genes and regions were selected for sequencing in order to identify all polymorphisms., and once the major haplotypes were determined, appropriate genomic DNA samples were selected such that each major haplotype and haplotype subset were represented in at least two to four copies. 3741 SNPs were identified, and once the major haplotypes were determined, appropriate genomic DNA samples were selected such that each major haplotype and haplotype subset were represented in at least two to four copies. The confirmation of putative assocns. was also performed in an independent general population patient sample. In particular, the invention relates to the fields of pharmacogenomics, diagnostics, patient therapy and the use of genetic haplotype information to predict an individual's longevity, their protection against age-related diseases, and/or their response to a particular drug or drugs.

L4 ANSWER 3 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:1344127 CAPLUS
DN 146:246444

TI Determinants for dephosphorylation of the RNA polymerase II C-terminal domain by Scp1

AU Zhang, Yan; Kim, Youngjun; Genoud, Nicolas; Gao, Jianmin; Kelly, Jeffery W.; Pfaff, Samuel L.; Gill, Gordon N.; Dixon, Jack E.; Noel, Joseph P.

CS Howard Hughes Medical Institute Jack H. Skirball Center for Chemical Biology and Proteomics, The Salk Institute for Biological Studies, La Jolla, CA, 92037, USA

SO Molecular Cell (2006), 24(5), 759-770
CODEN: MOCEFL; ISSN: 1097-2765

PB Cell Press

DT Journal

LA English

AB Phosphorylation and dephosphorylation of the C-terminal domain (CTD) of RNA polymerase II (Pol II) represent a critical regulatory checkpoint for transcription. Transcription initiation requires Fcpl/Scpl-mediated dephosphorylation of phospho-CTD. Fcpl and Scpl belong to a family of Mg²⁺-dependent phosphoserine (P.Ser)/phosphothreonine (P.Thr)-specific phosphatases. We recently showed that Scpl is an evolutionarily conserved regulator of neuronal gene silencing. Here, we present the x-ray crystal structures of a dominant-neg. form of human Scpl (D96N mutant) bound to mono- and diphosphorylated peptides encompassing the CTD heptad repeat (Y1S2P3T4S5P6S7). Moreover, kinetic and thermodyn. analyses of Scpl-phospho-CTD peptide complexes support the structures determined. This combined structure-function anal. discloses the residues in Scpl involved in CTD binding and its preferential dephosphorylation of P.Ser5 of the CTD heptad repeat. Moreover, these results provide a template for the design of specific inhibitors of Scpl for the study of neuronal stem cell development.

RE.CNT 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2005:100485 CAPLUS

DN 142:311908

TI Enhanced Binding of RNAP II CTD Phosphatase FCP1 to RAP74 Following CK2 Phosphorylation

AU Abbott, Karen L.; Renfrow, Matthew B.; Chalmers, Michael J.; Nguyen, Bao D.; Marshall, Alan G.; Legault, Pascale; Omichinski, James G.

CS Department of Biochemistry and Molecular Biology and Department of Chemistry, University of Georgia, Athens, GA, 30602, USA

SO Biochemistry (2005), 44(8), 2732-2745

CODEN: BICHAW; ISSN: 0006-2960

PB American Chemical Society

DT Journal

LA English

AB FCP1 (TFIIF-associated CTD phosphatase) is the first identified CTD-specific phosphatase required to recycle RNA polymerase II (RNAP II). FCP1 activity has been shown to be regulated by the general transcription factors TFIIF (RAP74) and TFIIB, protein kinase CK2 (CK2), and the HIV-1 transcriptional activator Tat. Phosphorylation of FCP1 by CK2 stimulates FCP1 phosphatase activity and enhances binding of RAP74 to FCP1. We have examined consensus CK2 phosphorylation sites (acidic residue n + 3 to serine or threonine residue) located immediately adjacent to both RAP74-binding sites of FCP1. We demonstrate that both of these consensus CK2 sites can be phosphorylated in vitro and that phosphorylation at either CK2 site results in enhanced binding of RAP74 to FCP1. The CK2 site adjacent to the RAP74-binding site in the central domain of FCP1 is phosphorylated at a single threonine site (T584). The CK2 site adjacent to the RAP74-binding site in the carboxyl-terminal domain can be phosphorylated at three successive serine residues (S942-S944), with phosphorylations at S942 and S944 both contributing to enhanced binding to RAP74. With the use of tandem Fourier transform-ion cyclotron resonance mass spectrometry (FT-ICR), we demonstrate that the phosphorylation of S942-S944 occurs in a semi-ordered fashion with the initial phosphorylation occurring at either S942 or S944 followed by a second phosphorylation to yield the S942/S944 diphosphorylated species. Using NMR spectroscopy, we identify and map chemical shift changes onto the solution structure of the carboxyl-terminal domain of RAP74 (RAP74436-517) on complexation of RAP74436-517 with phosphorylated FCP1 peptides. These results provide new functional and structural information on the role of

phosphorylation in the recognition of acidic-rich activation domains involved in transcriptional regulation, and bring insights into how CK2 and TFIIF regulate FCP1 function.

RE.CNT 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:393621 CAPLUS
DN 143:92968
TI Cloning and characterization of a novel RNA polymerase
II C-terminal domain phosphatase
AU Zheng, Huarui; Ji, Chaoneng; Gu, Shaohua; Shi, Binying; Wang, Jin; Xie, Yi; Mao, Yumin
CS State Key Laboratory of Genetic Engineering, Institute of Genetics, School of Life Sciences, Fudan University, Shanghai, 200433, Peop. Rep. China
SO Biochemical and Biophysical Research Communications (2005), 331(4), 1401-1407
CODEN: BBRC9; ISSN: 0006-291X
PB Elsevier
DT Journal
LA English
AB Reversible phosphorylation of RNA polymerase (RNAP) II's largest subunit C-terminal domain (CTD) is a key event during mRNA metabolism The CTD phosphatase, FCP1, catalyzes the dephosphorylation of RNAP II and is thought to play a major role in polymerase recycling. In this study, we isolated a novel phosphatase gene by large-scale sequencing anal. of a human fetal brain cDNA library. Its cDNA is 2215 bp in length, encoding a 318-amino acid polypeptide that contains a ubiquitin-like domain and a CTD phosphatase domain. Therefore, it was termed ubiquitin-like domain containing CTD phosphatase 1 (UBLCP1). Reverse transcription PCR (RT-PCR) revealed that UBLCP1 was expressed with relatively lower levels in most adult normal tissues and higher levels in fast growing or tumor tissues. Transient transfection experiment suggested that UBLCP1 was localized in the nucleus of COS-7 cells. Significantly, UBLCP1 could dephosphorylate GST-CTD in vitro. Accordingly, UBLCP1 may play a role in the regulation of phosphorylation state of RNA polymerase II C-terminal domain.

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:64569 CAPLUS
DN 142:293605
TI Identification of proteins interacting with the RNAPII FCP1 phosphatase: FCP1 forms a complex with arginine methyltransferase PRMT5 and it is a substrate for PRMT5-mediated methylation
AU Amente, Stefano; Napolitano, Giuliana; Licciardo, Paolo; Monti, Maria; Pucci, Piero; Lania, Luigi; Majello, Barbara
CS Department of Genetics, General and Molecular Biology, University of Naples 'Federico II' Naples, Naples, 80134, Italy
SO FEBS Letters (2005), 579(3), 683-689
CODEN: FEBLAL; ISSN: 0014-5793
PB Elsevier B.V.
DT Journal
LA English
AB FCP1, a phosphatase specific of the carboxyl-terminal-domain of the large subunit of the RNA polymerase II (RNAPII), stimulates transcription elongation and it is required for general transcription and cell viability. To identify novel interacting proteins of FCP1, we used a human cell line expressing an epitope flagged FCP1 and proteins, which formed complexes with FCP1, were identified by mass spectrometry. We identified four proteins: RPB2 subunit of the RNAPII, the nuclear kinase,

NDR1, the methyltransferase PRMT5 and the enhancer of rudimentary homolog (ERH) proteins. Intriguingly, both the PRMT5 and ERH proteins are interacting partners of the SPT5 elongation factor. Interactions of RPB2, ERH, NDR1 and PRMT5 with FCP1 were confirmed by co-immunopptn. or in vitro pull-down assays. Interaction between PRMT5 and FCP1 was further confirmed by co-immunopptn. of endogenous proteins. We found that FCP1 is a genuine substrate of PRMT5-methylation both in vivo and in vitro, and FCP1-associated PRMT5 can methylate histones H4 in vitro.

RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:67721 CAPLUS
DN 142:310802
TI Small CTD Phosphatases Function in Silencing Neuronal Gene Expression
AU Yeo, Michele; Lee, Soo-Kyung; Lee, Bora; Ruiz, Esmeralda C.; Pfaff, Samuel L.; Gill, Gordon N.
CS Department of Medicine, San Diego, University of California, La Jolla, CA, 92093, USA
SO Science (Washington, DC, United States) (2005), 307(5709), 596-600
CODEN: SCIEAS; ISSN: 0036-8075
PB American Association for the Advancement of Science
DT Journal
LA English
AB Neuronal gene transcription is repressed in non-neuronal cells by the repressor element 1 (RE-1)-silencing transcription factor/neuron-restrictive silencer factor (REST/NRSF) complex. To understand how this silencing is achieved, the authors examined a family of class-C RNA polymerase II (RNAPII) carboxyl-terminal domain (CTD) phosphatases [small CTD phosphatases (SCPs) 1 to 3], whose expression is restricted to non-neuronal tissues. The authors show that REST/NRSF recruits SCPs to neuronal genes that contain RE-1 elements, leading to neuronal gene silencing in non-neuronal cells. Phosphatase-inactive forms of SCP interfere with REST/NRSF function and promote neuronal differentiation of P19 stem cells. Likewise, small interfering RNA directed to the single Drosophila SCP unmasks neuronal gene expression in S2 cells. Thus, SCP activity is an evolutionarily conserved transcriptional regulator that acts globally to silence neuronal genes.

RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:878469 CAPLUS
DN 141:361557
TI Polynucleotide and polypeptide sequences for human SCP (small CTD phosphatase) phosphatases and uses thereof for regulating transcription, cell differentiation, and stem cells
IN Gill, Gordon N.; Yeo, Michele; Lin, Patrick S.; Dahmus, Michael E.
PA The Regents of the University of California, USA
SO PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DT Patent
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	WO 2004090098	A2	20041021	WO 2004-US10218	20040401
	WO 2004090098	A3	20060216		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,			

LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
 NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
 TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, US
 RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
 BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
 ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
 SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
 TD, TG

US 20070172470 A1 20070726 US 2006-552298 20060612

PRAI US 2003-459786P P 20030401

WO 2004-US10218 W 20040401

AB The invention provides nucleic acids, polypeptides, and methods for regulating the phosphorylation state of the C-terminal domain (CTD) of RNA polymerase II (RNAP II). Specifically, the invention claims sequences for human small CTD (C-terminal domain) phosphatases SCP1, SCP2, and SCP3. It also provides methods for regulating neuronal or stem cell differentiation by modulating SCP gene expression, for example with antisense oligonucleotides or siRNA, or by modulating SCP activity. Recombinant SCP1 phosphatase activity was abolished in the D95E/D97N double mutant using phosphorylated forms of CTD or RNA polymerase II as substrates. SCP2 showed comparable activity. SCP1 inhibited transcription of promoter-reporter gene constructs in HEK293, COS-7, and CV-1 cells, while the doubly mutant SCP1 enhanced transcription activity. SCP1 co-immunoprecipitated with RNA polymerase II and REST/NRSF complexes and was associated with REST binding sites of SCN2A2, GRIN2A, and GAD1 genes. Similar to REST/NRSF, SCP family mRNA was detected in non-neuronal tissues but was low or excluded from brain and neuronal tissues. Drosophila S2 cells treated with SCP siRNA showed enhanced expression of neuronal and glial genes.

L4 ANSWER 9 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2004:713803 CAPLUS

DN 141:362360

TI Structure and mechanism of RNA polymerase II CTD phosphatases

AU Kamenski, Tomislav; Heilmeyer, Susanna; Meinhardt, Anton; Cramer, Patrick

CS Department of Chemistry and Biochemistry Gene Center, University of Munich, Munich, 81377, Germany

SO Molecular Cell (2004), 15(3), 399-407

CODEN: MOCEFL; ISSN: 1097-2765

PB Cell Press

DT Journal

LA English

AB Recycling of RNA polymerase II (Pol II) after transcription requires dephosphorylation of the polymerase C-terminal domain (CTD) by the phosphatase Fcpl. We report the X-ray structure of the small CTD phosphatase Scpl, which is homologous to the Fcpl catalytic domain. The structure shows a core fold and an active center similar to those of phosphotransferases and phosphohydrolases that solely share a DXDX(V/T) signature motif with Fcpl/Scpl. We demonstrate that the first aspartate in the signature motif undergoes metal-assisted phosphorylation during catalysis, resulting in a phosphoaspartate intermediate that was structurally mimicked with the inhibitor beryll fluoride. Specificity may result from CTD binding to a conserved hydrophobic pocket between the active site and an insertion domain that is unique to Fcpl/Scpl. Fcpl specificity may additionally arise from phosphatase recruitment near the CTD via the Pol II subcomplex Rpb4/7, which is shown to be required for binding of Fcpl to the polymerase in vitro.

RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2003:647524 CAPLUS
 DN 139:229108
 TI Nuclear Protein Phosphatase-1 Regulates HIV-1 Transcription
 AU Ammosova, Tatyana; Jerebtsova, Marina; Beullens, Monique; Voloshin, Yaroslav; Ray, Patricio E.; Kumar, Ajit; Bollen, Mathieu; Nekhai, Sergei
 CS Center for Sickle Cell Disease, Howard University, Washington, DC, 20059, USA
 SO Journal of Biological Chemistry (2003), 278(34), 32189-32194
 CODEN: JBCHA3; ISSN: 0021-9258
 PB American Society for Biochemistry and Molecular Biology
 DT Journal
 LA English
 AB The authors recently reported that protein phosphatase 1 (PP1) dephosphorylates RNA polymerase II C-terminal repeats and regulates HIV-1 transcription in vitro. Here the authors provide evidence that PP1 is also required for Tat-induced HIV-1 transcription and for viral replication in cultured cells. Inhibition of PP1 by overexpression of nuclear inhibitor of PP1 (NIPPI) inhibited Tat-induced HIV-1 transcription in transient transfection assays. A mutant of NIPPI that was defective in binding to PP1 did not have this effect. Also the co-expression of PP1 reversed the inhibitory effect of NIPPI. Adeno-associated virus-mediated delivery of NIPPI significantly reduced HIV-1 transcription induced by Tat-expressing adenovirus in CD4+ HeLa cells that contained an integrated HIV-1 promoter (HeLa MAGI cells). In addition, infection of HeLa MAGI cells with adeno-associated virus-NIPPI prior to the infection with HIV-1 significantly reduced the level of HIV-1 replication. The authors' results indicate that PP1 might be a host cell factor that is required for HIV-1 viral transcription. Therefore, nuclear PP1 may represent a novel target for anti-HIV-1 therapeutics.

RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2003:524655 CAPLUS
 DN 139:193353
 TI A Novel RNA Polymerase II C-terminal Domain Phosphatase That Preferentially Dephosphorylates Serine 5
 AU Yeo, Michele; Lin, Patrick S.; Dahmus, Michael E.; Gill, Gordon N.
 CS Department of Medicine, University of California, San Diego, La Jolla, CA, 92093-0650, USA
 SO Journal of Biological Chemistry (2003), 278(28), 26078-26085
 CODEN: JBCHA3; ISSN: 0021-9258
 PB American Society for Biochemistry and Molecular Biology
 DT Journal
 LA English
 AB The transcription and processing of pre-mRNA in eukaryotic cells are regulated in part by reversible phosphorylation of the C-terminal domain of the largest RNA polymerase (RNAP) II subunit. The CTD phosphatase, FCP1, catalyzes the dephosphorylation of RNAP II and is thought to play a major role in polymerase recycling. This study describes a family of small CTD phosphatases (SCPs) that preferentially catalyze the dephosphorylation of Ser5 within the consensus repeat. The preferred substrate for SCP1 is RNAP II phosphorylated by TFIIH. Like FCP1, the activity of SCP1 is enhanced by the RAP74 subunit of TFIIIF. Expression of SCP1 inhibits activated transcription from a number of promoters, whereas a phosphatase-inactive mutant of SCP1 enhances transcription. Accordingly, SCP1 may play a role in the regulation of gene expression, possibly by controlling the transition from initiation/capping to processive transcript elongation.

RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2003:397602 CAPLUS
 DN 139:175406
 TI NMR structure of a complex containing the TFIIF subunit RAP74 and the RNA polymerase II carboxyl-terminal domain phosphatase FCP1
 AU Nguyen, Bao D.; Abbott, Karen L.; Potempa, Krzysztof; Kobor, Michael S.; Archambault, Jacques; Greenblatt, Jack; Legault, Pascale; Omichinski, James G.
 CS Departments of Biochemistry and Molecular Biology, University of Georgia, Athens, GA, 30602, USA
 SO Proceedings of the National Academy of Sciences of the United States of America (2003), 100(10), 5688-5693
 CODEN: PNASA6; ISSN: 0027-8424
 PB National Academy of Sciences
 DT Journal
 LA English
 AB FCP1 [transcription factor IIF (TFIIF)-associated carboxyl-terminal domain (CTD) phosphatase] is the only identified phosphatase specific for the phosphorylated CTD of RNA polymerase II (RNAP II). The phosphatase activity of FCP1 is enhanced in the presence of the large subunit of TFIIF (RAP74 in humans). It has been demonstrated that the CTD of RAP74 (cterRAP74; residues 436-517) directly interacts with the highly acidic CTD of FCP1 (cterFCP; residues 879-961 in human). In this manuscript, we have determined a high-resolution solution structure of a cterRAP74/cterFCP complex by NMR spectroscopy. Interestingly, the cterFCP protein is completely disordered in the unbound state, but forms an α -helix (H1'; E945-M961) in the complex. The cterRAP74/cterFCP binding interface relies extensively on van der Waals contacts between hydrophobic residues from the H2 and H3 helices of cterRAP74 and hydrophobic residues from the H1' helix of cterFCP. The binding interface also contains two critical electrostatic interactions involving aspartic acid residues from H1' of cterFCP and lysine residues from both H2 and H3 of cterRAP74. There are also three addnl. polar interactions involving highly conserved acidic residues from the H1' helix. The cterRAP74/cterFCP complex is the first high-resolution structure between an acidic residue-rich domain from a holoenzyme-associated regulatory protein and a general transcription factor. The structure defines a clear role for both hydrophobic and acidic residues in protein/protein complexes involving acidic residue-rich domains in transcription regulatory proteins.

RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2003:222959 CAPLUS
 DN 138:382630
 TI The FCP1 phosphatase interacts with RNA polymerase II and with MEP50 a component of the methylosome complex involved in the assembly of snRNP
 AU Licciardo, Paolo; Amente, Stefano; Ruggiero, Luca; Monti, Maria; Pucci, Piero; Lania, Luigi; Majello, Barbara
 CS Department of Genetics, General and Molecular Biology, University of Naples "Federico II", Naples, 80134, Italy
 SO Nucleic Acids Research (2003), 31(3), 999-1005
 CODEN: NARHAD; ISSN: 0305-1048
 PB Oxford University Press
 DT Journal
 LA English

AB RNA polymerase II transcription is associated with cyclic phosphorylation of the C-terminal domain (CTD) of the large subunit of RNA polymerase II. To date, FCP1 is the only specific CTD phosphatase, which is required for general transcription and cell viability. To identify FCP1-associated proteins, we constructed a human cell line expressing epitope-tagged FCP1. In addition to RAP74, a previously identified FCP1 interacting factor, we determined that FCP1-affinity purified exts. contain RNAPII that has either a hyper- or a hypo-phosphorylated CTD. In addition, by mass spectrometry of affinity purified FCP1-associated factors, we identified a novel FCP1-interacting protein, named MEP50, a recently described component of the methylosome complex that binds to the snRNP's Sm proteins. We found that FCP1 specifically interacts with components of the spliceosomal U small nuclear ribonucleoproteins. These results suggest a putative role of FCP1 CTD-phosphatase in linking the transcription elongation with the splicing process.

RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2003:963901 CAPLUS
DN 140:55364

TI Dephosphorylation of RNA Polymerase II by
CTD-phosphatase FCP1 is Inhibited by Phospho-CTD Associating
Proteins

AU Palancade, Benoit; Marshall, Nicholas F.; Tremereau-Bravard, Alexandre;
Bensaude, Olivier; Dahmus, Michael E.; Dubois, Marie-Francoise
CS Ecole Normale Supérieure, UMR 8541 CNRS, Genetique Moleculaire, Paris,
75230, Fr.

SO Journal of Molecular Biology (2003), Volume Date 2004, 335(2), 415-424
CODEN: JMOBAK; ISSN: 0022-2836

PB Elsevier

DT Journal

LA English

AB Reversible phosphorylation of the repetitive C-terminal domain (CTD) of the largest RNA polymerase (RNAP) II subunit plays a key role in the progression of RNAP through the transcription cycle. The level of CTD phosphorylation is determined by multiple CTD kinases and a CTD phosphatase, FCP1. The phosphorylated CTD binds to a variety of proteins including the cis/trans peptidyl-prolyl isomerase (PPIase) Pin1 and enzymes involved in processing of the primary transcript such as the capping enzyme Hc1 and CA150, a nuclear factor implicated in transcription elongation. Results presented here establish that the dephosphorylation of hyperphosphorylated RNAP II (RNAP IIO) by FCP1 is impaired in the presence of Pin1 or Hc1, whereas CA150 has no influence on FCP1 activity. The inhibition of dephosphorylation is observed with free RNAP IIO generated by different CTD kinases as well as with RNAP IIO engaged in an elongation complex. These findings support the idea that specific phospho-CTD associating proteins can differentially modulate the dephosphorylation of RNAP IIO by steric hindrance and may play an important role in the regulation of gene expression.

RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 20 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
STN

AN 2003:496505 BIOSIS
DN PREV200300486462

TI Partial deficiency of the C-terminal-domain phosphatase of
RNA polymerase II is associated with
congenital cataracts facial dysmorphism neuropathy syndrome.

AU Varon, Raymonda; Gooding, Rebecca; Steglich, Christina; Marns, Lorna;

Tang, Hua; Angelicheva, Dora; Yong, Kiau Kiun; Ambrugger, Petra; Reinhold, Anke; Morar, Bharti; Baas, Frank; Kwa, Marcel; Tournev, Ivailo; Guerguelcheva, Velina; Kremensky, Ivo; Lochmuller, Hanns; Mullner-Eidenbock, Andrea; Merlini, Luciano; Neumann, Luitgard; Burger, Joachim; Walter, Maggie; Swoboda, Kathryn; Thomas, P. K.; von Moers, Arpad; Risch, Neil; Kalaydjieva, Luba [Reprint Author]

CS Laboratory of Molecular Genetics, Western Australian Institute for Medical Research, University of Western Australia Centre for Medical Research, Perth, Australia
luba@cyllene.uwa.edu.au

SO Nature Genetics, (October 2003) Vol. 35, No. 2, pp. 185-189. print.
ISSN: 1061-4036 (ISSN print).

DT Article

LA English

OS DDBJ-NT010879.13; EMBL-NT010879.13; GenBank-NT010879.13

ED Entered STN: 22 Oct 2003

Last Updated on STN: 22 Oct 2003

AB Congenital cataracts facial dysmorphism neuropathy (CCFDN) syndrome (OMIM 604168) is an autosomal recessive developmental disorder that occurs in an endogamous group of Vlax Roma (Gypsies; refs. 1-3). We previously localized the gene associated with CCFDN to 18qter, where a conserved haplotype suggested a single founder mutation. In this study, we used recombination mapping to refine the gene position to a 155-kb critical interval. During haplotype analysis, we found that the non-transmitted chromosomes of some unaffected parents carried the conserved haplotype associated with the disease. Assuming such parents to be completely homozygous across the critical interval except with respect to the disease-causing mutation, we developed a new 'not quite identical by descent' (NQIBD) approach, which allowed us to identify the mutation causing the disease by sequencing DNA from a single unaffected homozygous parent. We show that CCFDN is caused by a single-nucleotide substitution in an antisense Alu element in intron 6 of CTDP1 (encoding the protein phosphatase FCP1, an essential component of the eukaryotic transcription machinery), resulting in a rare mechanism of aberrant splicing and an Alu insertion in the processed mRNA. CCFDN thus joins the group of 'transcription syndromes' and is the first 'purely' transcriptional defect identified that affects polymerase II-mediated gene expression.

L4 ANSWER 16 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2002:798436 CAPLUS

DN 138:102775

TI Protein Phosphatase-1 Dephosphorylates the C-terminal Domain of RNA Polymerase-II

AU Washington, Kareem; Ammosova, Tatyana; Beullens, Monique; Jerebtsova, Marina; Kumar, Ajit; Bollen, Mathieu; Nekhai, Sergei

CS Center for Sickle Cell Disease and Department of Biochemistry and Molecular Biology, Howard University, Washington, DC, 20059, USA

SO Journal of Biological Chemistry (2002), 277(43), 40442-40448
CODEN: JBCHA3; ISSN: 0021-9258

PB American Society for Biochemistry and Molecular Biology

DT Journal

LA English

AB Transcription by RNA polymerase-II (RNAPII) is controlled by multisite phosphorylation of the heptapeptide repeats in the C-terminal domain (CTD) of the largest subunit. Phosphorylation of CTD is mediated by the cyclin-dependent protein kinases Cdk7 and Cdk9, whereas protein serine/threonine phosphatase FCP1 dephosphorylates CTD. We have recently reported that human immunodeficiency virus-1 (HIV-1) transcription is pos. regulated by protein phosphatase-1 (PP1) and that PP1 dephosphorylates recombinant CTD. Here, we provide further evidence that PP1 can dephosphorylate RNAPII CTD. In vitro, PP1 dephosphorylated recombinant

CTD as well as purified RNAPII CTD. HeLa nuclear exts. were found to contain a species of PP1 that dephosphorylates both serine 2 and serine 5 of the heptapeptide repeats. In nuclear exts., PP1 and FCP1 contributed roughly equally to the dephosphorylation of serine 2. PP1 co-purified with RNAPII by gel filtration and associated with RNAPII on immunoaffinity columns prepared with anti-CTD antibodies. In cultured cells treated with CTD kinase inhibitors, the dephosphorylation of RNAPII on serine 2 was inhibited by 45% by preincubation with okadaic acid, which inhibits phosphatases of PPP family, including PP1 but not FCP1. Our data demonstrate that RNAPII CTD is dephosphorylated by PP1 in vitro and by PPP-type phosphatase, distinct from FCP1, in vivo.

RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2002:806230 CAPLUS

DN 138:217440

TI FCP1, a phosphatase specific for the heptapeptide repeat of the largest subunit of RNA polymerase II, stimulates transcription elongation

AU Mandal, Subhrangsu S.; Cho, Helen; Kim, Sungjoon; Cabane, Kettly; Reinberg, Danny

CS Division of Nucleic Acids Enzymology, Department of Biochemistry, Howard Hughes Medical Institute, Robert Wood Johnson Medical School, University of Medicine and Dentistry of New Jersey, Piscataway, NJ, 08854, USA

SO Molecular and Cellular Biology (2002), 22(21), 7543-7552

CODEN: MCEBD4; ISSN: 0270-7306

PB American Society for Microbiology

DT Journal

LA English

AB FCP1, a phosphatase specific for the carboxy-terminal domain of RNA polymerase II (RNAP II), was found to stimulate transcript elongation by RNAP II in vitro and in vivo. This activity is independent of and distinct from the elongation-stimulatory activity associated with transcription factor IIF (TFIIF), and the elongation effects of TFIIF and FCP1 were found to be additive. Genetic expts. resulted in the isolation of several distinct fcpl alleles. One of these alleles was found to suppress the slow-growth phenotype associated with either the reduction of intracellular nucleotide concns. or the inhibition of other transcription elongation factors. Importantly, this allele of fcpl was found to be lethal when combined individually with two mutations in the second-largest subunit of RNAP II, which had been shown previously to affect transcription elongation.

RE.CNT 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2002:403293 CAPLUS

DN 138:50681

TI A Protein Phosphatase from Human T Cells Augments Tat Transactivation of the Human Immunodeficiency Virus Type 1 Long-Terminal Repeat

AU Bharucha, Diana C.; Zhou, Meisheng; Nekhai, Sergei; Brady, John N.; Shukla, Ram R.; Kumar, Ajit

CS The George Washington University Medical Center, Department of Biochemistry and Molecular Biology, Washington, DC, 20037, USA

SO Virology (2002), 296(1), 6-16

CODEN: VIRLAX; ISSN: 0042-6822

PB Elsevier Science

DT Journal

LA English

AB HIV-1 Tat protein regulates viral gene expression by modulating the

activity and association of cellular transcription factors with RNA polymerase II (RNAPII). Possible mechanisms include Tat-associated protein kinase(s) and phosphatase(s) that regulate phosphorylation of the C-terminal domain (CTD) of the large subunit of RNAPII. Hypophosphorylated RNAPII (RNAPIIa) is recruited to promoters during formation of a preinitiation complex, whereas hyperphosphorylated RNAPII (RNAPIIo) is associated with the elongation complex. The role of phosphatases in maintaining the equilibrium between the two phosphorylated states of RNAPII, which is required for sustained transcriptional activation from the HIV-1 LTR, is not clear. In this study, the authors discuss the properties of a Tat-associated CTD phosphatase fractionated from Jurkat T cells. The Tat-associated protein phosphatase (TAPP) is related to the serine/threonine, type 1, protein phosphatase (PP1) family. TAPP dephosphorylates the hyperphosphorylated form of recombinant CTD specifically on serine 2, and augments Tat-mediated transcriptional transactivation of HIV-1 LTR in an in vitro transcription reaction. TAPP is associated with the transcription complex during the early initiation steps, and its release from the HIV-1 promoter coincides with the Tat-specific activation of CDK9. The results suggest a unique role of the Tat-associated phosphatase which regulates viral transcription by target-specific dephosphorylation of RNAPII during the early stages of elongation.

RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 19 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2000:471351 CAPLUS

DN 133:218392

TI Studies on the transcriptional regulation by human RNA polymerase II complexes and the CTD-phosphatase

AU Cho, Helen

CS Grad. Sch. of Biomed. Sci., Univ. of Medicine and Dentistry of N. J., NJ, USA

SO (1999) 173 pp. Avail.: UMI, Order No. DA9940679

From: Diss. Abstr. Int., B 2000, 60(7), 3112

DT Dissertation

LA English

AB Unavailable

L4 ANSWER 20 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN

AN 1999:437230 CAPLUS

DN 131:196148

TI A protein phosphatase functions to recycle RNA polymerase II

AU Cho, Helen; Kim, Tae-Kyung; Mancebo, Helena; Lane, William S.; Flores, Osvaldo; Reinberg, Danny

CS Howard Hughes Medical Institute, Division of Nucleic Acids Enzymology, Department of Biochemistry, Robert Wood Johnson Medical School, University of Medicine and Dentistry of New Jersey, Piscataway, NJ, 08854-5635, USA

SO Genes & Development (1999), 13(12), 1540-1552

CODEN: GEDEEP; ISSN: 0890-9369

PB Cold Spring Harbor Laboratory Press

DT Journal

LA English

AB Transcription is regulated by the state of phosphorylation of a heptapeptide repeat known as the carboxy-terminal domain (CTD) present in the largest subunit of RNA polymerase II (RNAPII). RNAPII that assoc. with transcription initiation complexes contains an unphosphorylated CTD, whereas the elongating polymerase has a phosphorylated CTD. Transcription factor IIH has a kinase activity specific for the CTD that is stimulated by the formation of a transcription initiation complex. Here, the authors report the isolation of a cDNA clone encoding a 150-kD polypeptide, which,

together with RNAPII, reconstitutes a highly specific CTD phosphatase activity. Functional anal. demonstrates that the CTD phosphatase allows recycling of RNAPII. The phosphatase dephosphorylates the CTD allowing efficient incorporation of RNAPII into transcription initiation complexes, which results in increased transcription. The CTD phosphatase was found to be active in ternary elongation complexes. Moreover, the phosphatase stimulates elongation by RNAPII; however, this function is independent of its catalytic activity.

RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD
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